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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/738,478	12/17/2003	Richard D. Cummings	5838.076	8217

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EXAMINER	
GAMBEL, PHILLIP	
ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
05/16/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/738,478	CUMMINGS ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 February 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 2 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 2 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment, filed 02/07/2007, has been entered.
Claim 3 has been canceled. Claim 1 has been canceled previously.
Claim 2 has been amended.

Claim 2 is pending.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.
This Action will be in response to applicant's amendment, filed 02/07/2007.
The rejections of record can be found the in the previous Office Action, mailed 12/18/2006.

3. Upon reconsideration of applicant's amended claims, the previous rejection under 35 U.S.C. § 112, second paragraph, has been withdrawn.

4. Claim 2 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention

Applicant's arguments in conjunction with the amended claims, filed 02/07/2007, have been fully considered as they apply to the rejection of record but have not been found convincing as it applies to the newly amended claims.

Applicant relies upon amending the claims to "methods of detecting defective binding between leukocytes and activated platelets or endothelial cells and measuring the binding of leucocytes obtained from a patient to anti-PSGL-1 antibodies" to obviate the rejection of record.

While applicant has deleted the recitation of "detecting a disorder involving defective binding of PSGL-1 in a patient" in the current claims,
the claims still read on "measuring the binding of leucocytes obtained from a patient" and the disclosed utilities are still drawn to detection of human disorders as described in paragraphs [0087] – [0092] in the Section of Diagnostic Reagents in the specification as filed.

With respect to disorders involving PSGL-1 as well as appropriate PSGL-1 specificities applicable for detection of defective binding,
the following of record has been noted.

In vitro and animal model studies have not correlated well with clinical diagnosis in patients. Since the detection of a disorder/disease can be disorder/disease-dependent, it is not clear that reliance on the in vitro and in vivo observations as well as the clinical experience with targeting various inflammatory conditions with anti-PSGL-1 antibodies accurately reflects the relative ability or efficacy of the claimed "methods to detect a defective binding between leukocytes and activated platelets or endothelial cells".

In a review on the Role of PSGL-1 Binding to Selectins in Leukocyte Recruitment in McEver and Cummings, J. Clin. Invest. 100: S97-S103, 1997;

the co-inventors conclude that:

"Many interesting questions remained to be answered. These include defining the details of the post-translational modifications that confer optimal PSGL-1 binding to selectins, the nature of the molecular contacts between lectin and ligand, the biophysical parameters that facilities cell-cell interactions under flow, the molecular mechanism for PSGL-1-mediated leukocyte signaling and the role of PSGL-1-selectin interactions in vivo during physiological and pathological inflammation, hemostasis and hematopoiesis."

See entire document, including Conclusions on page S102.

Further, this J. Clin. Invest. Reference notes the broad Tissue Distribution of PSGL-1, including the observations that PSGL-1 is expressed differentially on leukocytes and this expression may differ in the same cell populations or that the PSGL-1 may be modified differentially among the leukocytes.

See Tissue Distribution of PSGL-1 on page S100.

Several variables are used in evaluating the predictability of detection or diagnostic assays. These include diagnostic specificity and sensitivity and positive and negative predictive values.

The diagnostic sensitivity of an assay reflects the fraction of those subjects with a specific disease that the assay correctly identifies as positive.

The diagnostic specificity of an assay reflects the fraction of those subjects without the disease that the assay correctly identifies as negative.

The positive predictive value refers to the probability that an individual with a positive test result has the disease.

The negative predictive value refers to the probability that an individual with a negative test result does not have the disease.

There is an inverse relationship between the sensitivity and specificity, which is related to the assigned cutoff value that is used for a particular test to segregate diseased populations from those with no disease.

Given the various modifications conferring PSGL-1-mediated binding as well as the differential expression of PSGL-1 on leukocytes,

The instant specification does not appear to provide sufficient guidance and direction as to those PSGL-1 specificities that would be appropriate for detecting defects of PSGL-1 in any type of leukocyte.

Both the anti-PSGL-1 antibody specificities and the type of leukocyte appear to be variables not accounted for by the instant claims and specification.

For example, antibodies to the carbohydrate determinants or the protein determinants not involved in leukocyte binding would not appear to be enabled.

Again, given the variables of both the nature of the PSGL-1 expressed on leukocytes as well as the differential expression of PSGL-1 on different types of leukocytes,

it would have been unpredictable at the time to detect defective binding between leukocytes and PSGL-1 as broadly claimed.

In the absence of objective evidence to the contrary and keeping with the nature of evaluating a number of potential PSGL-1 antigenic specificities for detection of defective binding of any leukocyte expressing PSGL-1,

the skilled artisan would predict that there is an overlap between defective and non-defective expression of PSGL-1 on leukocytes, since different leucocytes exhibit PSGL-1 differentially and the nature of the PSGL-1 on a leukocyte can also vary.

Therefore, anti-PSGL-1 antibodies of varying specificities (e.g., protein, carbohydrate moieties) may or may not detect defective binding between leukocytes and activated platelets or endothelial cells, because the specificity of the anti-PSGL-1 antibody may not be appropriate.

The lack of binding by an anti-PSGL-1 antibody may be due to the inappropriate anti-PSGL-1 specificity as well as due to the inappropriate leukocyte involved in the assay.

Given the lack of structure – function correlation as to those particular components / epitopic specificities of PSGL-1 that are involved in leukocyte binding as they read on both the anti-PSGL-1 antibodies and the scope of leukocytes, the skilled artisan would not predicted that any anti-PSGL-1 antibody could detect defective PSGL-1 on any leukocyte.

Further, it appears the current assay relies only the binding of anti-PSGL-1 antibodies to various leukocytes to determine a functional endpoint of leukocyte binding to platelets or endothelial cells.

There is insufficient objective evidence that determining expression of PSGL-1 with any anti-PSGL-1 antibody specificity alone would confer predictability of a functional or bioassay of leucocytes binding to platelets or endothelial cells.

Here, applicant has not provided sufficient direction and guidance as to the sensitivity and specificity of detecting defective binding of P-selectin glycoprotein ligand via the use of any PSGL-1-specific antibody.

There is insufficient objective evidence that the claimed assay which relies upon the detection of PSGL-1 on various types of leukocytes obtained from various patients provides the requisite sensitivity and specificity to be useful for the claimed purpose detecting defective binding of P-selectin glycoprotein ligand via the use of any PSGL-1-specific antibody alone.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth.

In view of the lack of predictability of the art to which the invention pertains the lack of established protocols for effective methods to detecting defective expression of PSGL-1 in any type of leukocyte with any specificity of any PSGL-1-specific antibody-based assays, undue experimentation would be required to practice the claimed methods of detecting defective binding of PSGL-1 with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed methods and absent working examples providing evidence which is reasonably predictive that the claimed methods are effective for detecting defective binding between leukocytes and activated platelets or endothelial cells via monitoring a patient's leukocytes with PSGL-1-specific antibodies alone, broadly encompassed by the claimed methods.

In response to this rejection, applicant is invited to consider as to whether the anti-PSGL-1 antibodies need to bind specific portions of PSGL-1 (e.g., receptor-ligand regions PSGL-1 involved in leukocyte binding) or specific types of PSGL-1 (e.g., post-translational modifications) in order to carry out the claimed methods.

5. No claim is allowed.

6. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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May 14, 2007